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Substitute for form 1449A/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Application Number	Divisional of 09/182,616
		09/378,261	09/182,616
		Filing Date	August 20, 1999
		First Named Inventor	Kenji Fukudome
		Group Art Unit	1647
		Examiner Name	Not Yet Assigned
		Attorney Docket Number	OMRF 152 DIV(3)
Sheet	1	of	14

U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	US Patent Document		Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code ² (if known)			
56	3,625,214			Higuchi	12-07-1971	
"	4,244,946			Rivier	01-13-1981	
"	4,305,872			Johnston, et al.	12-15-1981	
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"	4,782,137			Hopp, et al.	11-01-1988	
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"	4,925,673			Steiner, et al.	05-15-1990	
"	4,980,286			Morgan, et al.	12-25-1990	
"	5,009,889			Taylor, et al.	04-23-1991	
"	5,298,599			Rezaie, et al.	03-29-1994	
"	5,695,993			Fukudome, et al.	12-09-1997	
"	5,698,189			Rowe, et al.	12-16-1997	
"	5,749,968			Melanson, et al.	05-12-1998	
"	5,779,673			Roth, et al.	07-14-1998	
"	5,804,392			Esmon, et al.	09-08-1998	

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Examiner Initials*	Cite No. ¹	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Office ³	Number ⁴	Kind Code ⁵ (if known)				
56	WO	96/05303			Oklahoma Med. Res. Found.	02-22-1996		
"	WO	96/20732			Chiron Viagene	07-11-1996		
"	WO	96/21470			Genemedicine, Inc.	07-18-1996		
"	WO	98/20041			Oklahoma Med. Res. Found	05-14-1998		
"								

Examiner Signature	<i>Stephen Jucker</i>	Date Considered	7/15/01
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OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, cit and/or country where published	T ²
S6		ABE, et al., "Granulocyte proteases and hydrogen peroxide synergistically inactive thrombomodulin of endothelial cells in vitro," <i>J. Lab. Clin. Med.</i> 123(6):874-881 (1994).	
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S6		BOEHME, et al., "Release of thrombomodulin from endothelial cells by concentrated action of TNF- α and neutrophils: <i>in vivo</i> and <i>in vitro</i> studies," <i>Immunology</i> 87:134-140 (1996).	
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Sheet	4	of	14

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S8		DITTMAN & MAJERUS, "Structure and Function of Thrombomodulin: A Natural Anticoagulant," <i>Blood</i> 75(2):329-336 (1990).	
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Sheet	5	of	14		

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SF		ESMON, "Protein S and Protein C - Biochemistry, Physiology, and Clinical Manifestation of Deficiencies," <i>Trends Cardiovasc. Med.</i> 2(6):214-220 (1992).	
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56		GREGORIADIS, "Liposomes," in <i>Drug Carriers in Biology and Medicine</i> , Chap. 14. pp. 287-341 (Academic Press, 1979).	
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		09/378,261	
		Filing Date	August 20, 1999
		First Named Inventor	Kenji Fukudome
		Group Art Unit	169
		Examiner Name	Not Yet Assigned
Sheet	8	of	14
		Attorney Docket Number	OMRF 152 DIV(3)

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, cit and/or country where published	T ²
S6		LASZIK, et al., "The Human Protein C Receptor Is Present Primarily on Endothelium of Large Blood Vessels," <i>Circulation</i> , 96(10):1-9 (1997).	
ll		LE BONNIEC, et al., "The role of calcium ions in factor X activation by thrombin E192Q," <i>J Biol Chem</i> 267(10):6970-6 (1992).	
ll		LEDBETTER, et al., "Covalent association between human thymus leukemia-like antigens and CD8(Tp32) molecules," <i>J Immunol</i> 134(6):4250-4 (1985).	
ll		LENTZ, et al., "Regulation of Thrombomodulin by Tumor Necrosis Factor- α : Comparison of Transcriptional and Posttranscriptional Mechanisms," <i>Blood</i> 77(3):543-550, (1991).	
q		LEWIS, et al., "Automated site-directed drug design: the concept of spacer skeletons for primary structure generation," <i>Proc. R. Soc. Lond.</i> , 236(1283):125-140 (1989)	
ll		LEWIS, et al., "Automated site-directed drug design: the formation of molecular templates in primary structure generation," <i>Proc. R. Soc. Lond.</i> , 236(1283):141-162 (1989)	
ll		LOBIE, et al., "Nuclear translocation and anchorage of the growth hormone receptor," <i>J. Biol. Chem.</i> 269:31735-31746 (1994).	
ll		LU, et al., "The Active Site of the Thrombin-Thrombomodulin Complex - A Fluorescence Energy Transfer Measurement of its Distance Above the Membrane Surface," <i>J. Biol. Chem.</i> 264(22):12956-12962 (1989).	
ll		LUST, et al., "Isolation of An mRNA Encoding a Soluble Form of the Human Interleukin-6 Receptor," <i>Cytokine</i> 4(2):96-100 (1992).	
q		MACIAG, et al., "An endothelial cell growth factor from bovine hypothalamus: identification and partial characterization," <i>Proc Natl Acad Sci U S A.</i> 76(11):5674-8 (1979).	

Examiner's Signature	<i>Stephanie Gucke</i>	Date Considered	7/15/01
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Substitute for form 1449A/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Application Number 09/378,261	Divisional of 09/182,616
Filing Date First Named Inventor Group Art Unit Examiner Name	August 20, 1999 Kenji Fukudome Not Yet Assigned Not Yet Assigned		
Sheet 9 of 14	Attorney Docket Number	OMRF 152 DIV(3)	

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SG		MAHER, et al., "Inhibition of DNA binding proteins by oligonucleotide-directed triple helix formation," <i>Science</i> 245(4919):725-30 (1989).	
ll		MAHER, "Nuclear Translocation of fibroblast growth factor (FGF) receptors in response to FGF-2," <i>J. Cell Biol.</i> 134:529-536 (1996).	
ll		MARUYAMA, et al., "Increased expression of thrombomodulin on the cultured human umbilical vein endothelial cells and mouse hemangioma cells by cyclic AMP," <i>Thromb Res.</i> 61(3):301-10 (1991).	
ll		MATHER, et al., "The 2.8 Å Crystal Structure of Gla-Domainless Activated Protein C," <i>EMBO J.</i> 15(24):6822-6831 (1996).	
ll		MATHEWS, "Structure of a Nonadecapeptide of the Fifth EGF Domain of Thrombomodulin Complexed with Thrombin," <i>Biochemistry</i> 33:13547-13552 (1994).	
ll		MCKINLAY, et al., "Rational Design of Antiviral Agents," <i>Annual Review of Pharmacology and Toxicology</i> , 29:111-122 (1989)	
cl		MERRIFIELD, "Solid-Phase Peptide Synthesis. I. The Synthesis of a Tetrapeptide," <i>J. Am. Chem. Soc.</i> 85:2149-2154 (1964).	
cl		MIZUSHIMA, et al., "pEF-BOS, a powerful mammalian expression vector," <i>Nucleic Acids Res.</i> 18(17):5322 (1990).	
cl		MOORE, et al., "Tumor Necrosis Factor Leads to the Internalization and Degradation of Thrombosis from the Surface of Bovine Aortic Endothelial Cells in Culture," <i>Blood</i> 73(1):159-165 (1989).	
cl		MÜLLBERG, et al., "The Soluble Human IL-6 Receptor," <i>J. Immunol.</i> 152:4958-4968 (1994).	

Examiner's Signature	<i>Stephen Gucker</i>	Date Considered	7/15/01
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		09/378,261	
		Filing Date	August 20, 1999
		First Named Inventor	Kenji Fukudome
		Group Art Unit	Not Yet Assigned
		Examiner Name	Not Yet Assigned
Sheet	10	of	14
		Attorney Docket Number	OMRF 152 DIV(3)

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S6		MULLIGAN, et al., "The basic science of gene therapy," <i>Science</i> 260(5110):926-32 (1993)	
11		NARANG, et al., "Chemical Synthesis of Deoxyoligonucleotides by the Modified Triester Method," in <i>Methods Enzymol.</i> 65:610-620 (1980).	
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11		OHDAMA, et al., "Plasma Thrombomodulin in Wegener's Granulomatosis as an Indicator of Vascular Injuries," <i>Chest</i> 106:666-671 (1994).	
11		OLSEN, et al., "Ca2+ dependence of the interactions between protein C, thrombin, and the elastase fragment of thrombomodulin. Analysis by ultracentrifugation," <i>Biochemistry</i> 31(3):746-54 (1992).	
11		ORSON, et al., "Oligonucleotide inhibition of IL2R alpha mRNA transcription by promoter region collinear triplex formation in lymphocytes," <i>Nucleic Acids Res</i> 19(12):3435-41 (1991).	
11		OWEN, et al., "The Conversion of Prothrombin to Thrombin," <i>J. Biol. Chem.</i> 249(2):594-605 (1974).	
4		PANJA, et al., "CD1d is involved in T cell-intestinal epithelial cell interactions," <i>J Exp Med.</i> 178(3):1115-9 (1993).	
11		PARKINSON, et al., "Stable Expression of a Secretable Deletion Mutant of Recombinant Human Thrombomodulin in Mammalian Cells," <i>J. Biol. Chem.</i> 265(21):12602-12610 (1990).	
11		PERRY & DAVIES, <u>QSAR: Quantitative Structure-Activity Relationships in Drug Design</u> pp. 189-193 (Alan R. Liss, Inc. 1989)	

Examiner's Signature	Stephen Sander	Date Considered	7/15/01
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		Filing Date <i>August 20, 1999</i>	First Named Inventor <i>Kenji Fukudome</i>
		Group Art Unit <i>Not Yet Assigned</i>	Examiner Name <i>Not Yet Assigned</i>
Sheet	11	of	14
		Attorney Docket Number	OMRF 152 DIV(3)

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, cit and/or country where published	T ²
<i>SG</i>	PORCELLI, et al., "CD1b restricts the response of human CD4-8- T lymphocytes to a microbial antigen," <i>Nature</i> . 360(6404):593-7 (1992).		
<i>ll</i>	POSTEL, et al., "Evidence that a triplex-forming oligodeoxyribonucleotide binds to the c-myc promoter in HeLa cells, thereby reducing c-myc mRNA levels," <i>Proc Natl Acad Sci U S A</i> . 88(18):8227-31 (1991).		
<i>ll</i>	PROUDFOOT, et al., "3' non-coding region sequences in eukaryotic messenger RNA," <i>Nature</i> 263(5574):211-4 (1976).		
<i>ll</i>	QUEHENBERGER, et al., "Increased Levels of Activated Factor VII and Decreased Plasma Protein S Activity and Circulating Thrombomodulin During Use of Oral Contraceptives," <i>Thromb. Haemost.</i> 76:729-734 (1996).		
<i>ll</i>	REGAN, et al., "The endothelial cell protein C receptor. Inhibition of activated protein C anticoagulant function without modulation of reaction with proteinase inhibitors," <i>J. Biol. Chem.</i> 271, 17499-17503 (1996).		
<i>ll</i>	REITSMA, et al., "Protein C Deficiency: A Database of Mutations, 1995 Update," <i>Thromb. Haemost.</i> 73:876-879 (1995).		
<i>ll</i>	REZAI, et al., "Communication: Protein C Inhibitor Is a Potent Inhibitor of the Thrombin-Thrombomodulin Complex," <i>J. Biol. Chem.</i> 270(43):25336-25339 (1995).		
<i>ll</i>	RIPKA, "Computers Picture the Perfect Drug," <i>New Scientist</i> , 54-57 (June 16, 1988)		
<i>ll</i>	ROLLINS, et al., "Inhibition of Homologous Complement by CD59 is Mediated by a Species-Selective Recognition Conferred Through Binding to C8 Within C5b-8 or C9 Within C5b-9," <i>J. Immunol.</i> 146(7):2345-2351 (1991).		
<i>ll</i>	ROTHBARTH, et al., "cDNA-derived molecular characteristics and antibodies to a new centrosome-associated and G2/M phase-prevalent protein," <i>J Cell Sci.</i> 104 (Pt 1):19-30 (1993.).		

Examiner's Signature	<i>Stephen Buckley</i>	Date Considered	<i>7/15/01</i>
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Filing Date <i>August 20, 1999</i>	First Named Inventor <i>Kenji Fukudome</i>	Group Art Unit <i>1647</i>	Not Yet Assigned
Examiner Name <i></i>	Attorney Docket Number <i>OMRF 152 DIV(3)</i>		
Sheet	12	of	14

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
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<i>SC</i>		SADLER, et al., "Structure-Function Relationships of the Thrombin-Thrombomodulin Interaction," <i>Haemostasis</i> 23(suppl 1):183-193 (1993).	
<i>LC</i>		SARIN, et al., "Inhibition of acquired immunodeficiency syndrome virus by oligodeoxynucleoside methylphosphonates," <i>Proc. Natl. Acad. Sci. USA</i> 85(20):7448-7794 (1989).	
<i>CC</i>		SEBESTYÉN, et al., "DNA vector chemistry: the covalent attachment of signal peptides to plasmid DNA," <i>Nature Biotechnology</i> 16, 80-85 (1998).	
<i>CC</i>		SELIGSOHN, et al., "Homozygous Protein C Deficiency Manifested by Massive Venous Thrombosis in the Newborn," <i>N. Engl. J. Med.</i> 310(9):559-562 (1984).	
<i>CC</i>		SHAW, et al., "Modified deoxyoligonucleotides stable to exonuclease degradation in serum," <i>Nucleic Acids Res.</i> 19(4):747-750 (1991).	
<i>CC</i>		STEARNS, et al., "The Interaction of a Ca ²⁺ -dependent Monoclonal Antibody with the Protein C Activation Peptide Region," <i>J. Biol. Chem.</i> 263(2):826-832 (1988).	
<i>CC</i>		STEARNS-KUROSAWA, et al., "The endothelial cell protein C receptor augments protein C activation by the thrombin-thrombomodulin complex," <i>Proc. Natl. Acad. Sci. (USA)</i> 93:10212-10216 (1996).	
<i>CC</i>		STERN, et al., "Cultured bovine aortic endothelial cells promote activated protein C-protein S-mediated inactivation of factor Va," <i>J Biol Chem</i> 261(2):713-8 (1986).	
<i>CC</i>		SUZUKI, et al., "Structure and expression of human thrombomodulin, a thrombin receptor on endothelium acting as a cofactor for protein C activation," <i>EMBO J.</i> 6(7):1891-1897 (1987).	
<i>CC</i>		SZOSTAK, "In Vitro genetics," <i>TIBS</i> 19:89-93 (1992).	

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		Filing Date	August 20, 1999
		First Named Inventor	Kenji Fukudome
		Group Art Unit	1697 Not Yet Assigned
		Examiner Name	Not Yet Assigned
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<i>SB</i>		TAKAHASHI, et al., "Circulating Thrombomodulin As a Novel Endothelial Cell Marker: Comparison of Its Behavior with von Willebrand Factor and Tissue Type Plasminogen Activator," <i>Am. J. Hematol.</i> 41:32-39 (1992).	
<i>ll</i>		TAKAHASHI, et al., "Circulating Thrombomodulin in Thrombotic Thrombocytopenic Purpura," <i>Am. J. Hematol.</i> 38:174-177 (1991).	
<i>ll</i>		TAKANO, et al., "Plasma Thrombomodulin in Health and Diseases," <i>Blood.</i> 76(10):2024-2029 (1990).	
<i>ll</i>		TANAKA, et al., "Increased Thrombomodulin Values in Plasma of Diabetic Men with Microangiopathy," <i>Clin. Chem.</i> 37(2):269-272 (1991).	
<i>cl</i>		TAYLOR, et al., "C4b-Binding Protein Exacerbates the Host Response to <i>Escherichia coli</i> ," <i>Blood</i> 78(2):357-363 (1991).	
<i>cl</i>		TAYLOR, et al., "Protein C Prevents the Coagulopathic and Lethal Effects of <i>Escherichia coli</i> Infusion in the Baboon," <i>J. Clin. Invest.</i> 79:918-925 (1987).	
<i>ll</i>		VON HEIJNE, "A New Method for Predicting Signal Sequence Cleavage Sites," <i>Nucleic Acids Res.</i> 14(11):4683-4690 (1986).	
<i>ll</i>		WADA, et al., "Plasma Thrombomodulin as a Marker of Vascular Disorders in Thrombotic Thrombocytopenic Purpura and Disseminated Intravascular Coagulation," <i>Am. J. Hematol.</i> 39:20-24 (1992).	
<i>ll</i>		WEN, et al., "Human Thrombomodulin: Complete cDNA Sequence and Chromosome Localization of the Gene," <i>Biochemistry</i> 26:4350-4357 (1987).	
<i>ll</i>		WICKSTROM, et al., "Human promyelocytic leukemia HL-60 cell proliferation and c-myc protein expression are inhibited by an antisense pentadecadeoxynucleotide targeted against c-myc mRNA," <i>Proc Natl Acad Sci U S A.</i> 85(4):1028-32 (1988).	

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09/378,261		Filing Date	August 20, 1999
		First Named Inventor	Kenji Fukudome
		Group Art Unit	1697
		Examiner Name	Not Yet Assigned
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S6		WILLIAMS, et al., The immunoglobulin superfamily-domains for cell surface recognition., <i>Annu Rev Immunol</i> 6:381-405 (1988).	
11		XIE, et al., "Nuclear localization of p185neu tyrosine kinase and its association with transcriptional transactivation," <i>Biochem. Biophys. Res. Comm.</i> 203:1589-1598 (1994).	
11		YE, et al., "The Active Site of Thrombin is Altered Upon Binding to Thrombomodulin – Two Distinct Structural Changes are Detected by Fluorescence, but only one Correlates with Protein C Activation," <i>J. Biol. Chem.</i> 266(34):23016-23021 (1991).	
11		YE, et al., "The Fifth and Sixth Growth Factor-like Domains of Thrombomodulin Bind to the Anion-binding Exosite of Thrombin and Alter Its Specificity," <i>J. Biol. Chem.</i> 267(16):11023-11028 (1992).	
11		YOUNG, et al., "Triple helix formation inhibits transcription elongation in vitro," <i>Proc Natl Acad Sci U S A.</i> 88(22):10023-6 (1991).	
11		ZAMECNIK, et al., "Inhibition of replication and expression of human T-cell lymphotropic virus type III in cultured cells by exogenous synthetic oligonucleotides complementary to viral RNA," <i>Proc Natl Acad Sci U S A.</i> 83(12):4143-6 (1986).	
11		ZAMECNIK, et al., "Inhibition of Rous sarcoma virus replication and cell transformation by a specific oligodeoxynucleotide," <i>Proc Natl Acad Sci U S A.</i> 75:280-284 (1978).	

Examiner's Signature	Stephen Jucker	Date Considered	7/15/01
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